

Time with Diabetes Distress and Glycemia-specific Distress: New patient-reported outcome measures for the psychosocial burden of diabetes using ecological momentary assessment in an observational study.

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Supplementary Table S1. Reliability of the daily assessment of diabetes distress using multilevel confirmatory factor analysis.

PAID item used in EMA	Factor loading	Residual variance	Reliability measure Omega*
Within level			
feeling overwhelmed	0.704	0.504	0.76
feeling left alone	0.542	0.706	
taking up too much mental and physical energy	0.702	0.507	
feeling guilty or anxious when getting off track with diabetes management	0.429	0.816	
feelings of deprivation	0.670	0.550	
Between level			
feeling overwhelmed	0.910	0.172	0.92
feeling left alone	0.773	0.403	
taking up too much mental and physical energy	0.886	0.216	
feeling guilty or anxious when getting off track with diabetes management	0.752	0.434	
feelings of deprivation	0.868	0.246	
Two-level confirmatory factor analysis with all PAID items loading on one factor, controlled for study day and autoregressive parameter 1, with participant as nesting factor. Root Mean Square Error Of Approximation (RMSEA): 0.035; Comparative Fit Index (CFI): 0.978; Tucker-Lewis Index (TLI): 0.944 * Omega is calculated as the ratio of the squared sum of the factor loadings divided by the sum of the error variances added to the squared sum of factor loadings.(25)			

Supplementary Table S2. Reliability of daily glycemia-specific distress ratings averaging across all EMA days.

Source of Variance	Daily hypoglycemia distress	Daily hyperglycemia distress	Daily glucose variability distress
σ_{Person}^2	1.267	2.92	2.807
$\sigma_{Study\ day}^2$	0.031	0.07	0.049
σ_{Error}^2	5.202	6.812	5.425
<i>Reliability of between-person differences averaging across all days</i>			
Reliability estimate*	0.81	0.88	0.90
As single items were used, multilevel confirmatory factor analysis was not applicable. Thus, variance components for mixed models were estimated. All variance component estimates were based on 17 EMA days. * Reliability estimates were calculated as the ratio of person-level variance divided by the error variance per day added to the person-level variance.(26)			

Supplementary Table S3. Person level: Associations between Time with Diabetes Distress, Time with Glycemia-specific distresses and variables at the end of the EMA period and 3-month follow-up.

Follow-up variable	Mean daily distress ratings (over the 17-day EMA phase)				Time with distress (over the 17-day EMA phase): % of days with elevated ratings (≥ 40)			
	Mean daily diabetes distress (range: 0-100)	Mean daily hypoglycemia distress (range: 0-100)	Mean daily hyperglycemia distress (range: 0-100)	Mean daily glucose variability distress (range: 0-100)	Diabetes Distress	Hypoglycemia distress	Hyperglycemia distress	Glucose variability distress
<i>Patient-reported outcome at the end of the EMA period (n=178)</i>								
Diabetes Distress (PAID sum score, range:0-100)	0.64 (p < 0.001)	0.25 (p = 0.001)	0.39 (p < 0.001)	0.44 (p < 0.001)	0.57 (p < 0.001)	0.27 (p < 0.001)	0.32 (p < 0.001)	0.39 (p < 0.001)
<i>Patient-reported outcomes at 3-month follow-up (n=163)</i>								
Diabetes Distress (PAID sum score, range: 0-100)	0.61 (p < 0.001)	0.20 (p = 0.010)	0.35 (p < 0.001)	0.40 (p < 0.001)	0.52 (p < 0.001)	0.20 (p = 0.011)	0.31 (p < 0.001)	0.37 (p < 0.001)
Depressive Symptoms (CES-D sum score, range: 0-60)	0.32 (p < 0.001)	0.19 (p = 0.018)	0.08 (p = 0.328)	0.21 (p = 0.008)	0.25 (p = 0.001)	0.17 (p = 0.027)	0.07 (p = 0.386)	0.17 (p = 0.035)
Hypoglycemia Fear (HFS-II-SF sum score, range: 0-44)	0.46 (p < 0.001)	0.20 (p = 0.011)	0.31 (p < 0.001)	0.29 (p < 0.001)	0.36 (p < 0.001)	0.20 (p = 0.011)	0.29 (p < 0.001)	0.29 (p < 0.001)
Fear of complications	0.38 (p < 0.001)	0.21 (p = 0.006)	0.22 (p = 0.006)	0.26 (p = 0.001)	0.36 (p < 0.001)	0.22 (p = 0.006)	0.18 (p = 0.024)	0.23 (p = 0.003)

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Supplementary Table S4: Comparison of associations between diabetes distress (questionnaire vs. ecological momentary assessment) and glycemic management at follow-up.

CGM-derived glycemic parameters during the 14-day period at the 3-month follow-up	Questionnaire assessment at the end of the EMA period		Ecological momentary assessment	
	Diabetes Distress (PAID sum score)	Diabetes Distress short form (5 PAID questions used in the EMA-period)	Mean daily distress ratings (over the whole EMA period)	Time with distress (over the whole EMA period): % of days with elevated ratings (≥ 40)
Mean Glucose	0.07 (p = 0.391)	0.10 (p = 0.249)	0.22 (p = 0.005)	0.27 (p = 0.001)
Glucose variability (CV)	-0.10 (p = 0.245)	-0.09 (p = 0.256)	0.09 (p = 0.247)	0.06 (p = 0.430)
% <70 mg/dl (3.9 mmol/l)	-0.15 (p = 0.065)	-0.19 (p = 0.022)	-0.10 (p = 0.201)	-0.10 (p = 0.201)
% 70-180 mg/dl (3.9-10 mmol/l)	-0.01 (p = 0.885)	-0.02 (p = 0.796)	-0.17 (p = 0.030)	-0.20 (p = 0.014)
% >180 mg/dl (10 mmol/l)	0.04 (p = 0.596)	0.06 (p = 0.466)	0.18 (p = 0.025)	0.20 (p = 0.012)
HbA1c	0.09 (p = 0.253)	0.11 (p = 0.182)	0.23 (p = 0.005)	0.27 (p = 0.001)
N = 155. EMA = Ecological momentary assessment; CV = coefficient of variation; PAID = Problem Area in Diabetes questionnaire				

Supplementary Table S5. Drop-out analysis

	Participants included in analyses (n = 178)	Drop-out because of low adherence (n=25)	p-value
Age (in years)	39.0 ± 12.6	35.2 ± 14.4	0.163
Female gender	103 (58%)	16 (64%)	0.562
Body-mass index (in kg/m ²)	26.2 ± 5.1	25.7 ± 5.5	0.686
Years of education	13.2 ± 2.6	12.3 ± 2.6	0.117
Duration of diabetes (in years)	19.0 ± 11.7	15.5 ± 11.4	0.160
HbA1c (in %, [mmol/mol])	8.6 ± 1.9 [70 ± 21]	9.1 ± 1.9 [76 ± 21]	0.257
Insulin pump therapy	104 (58%)	14 (56%)	0.819
CGM [#] use prior to inclusion	152 (85%)	22 (88%)	0.729
Long-term complications ⁺ (mean per person)	0.71 ± 0.85	0.56 ± 0.82	0.416
<i>Patient-reported outcomes (Baseline assessment)</i>			
Diabetes distress (PAID sum score, range: 0-100)	39.9 ± 18.1	40.2 ± 18.4	0.950
Depressive symptoms (CES-D sum score, range: 0-60)	21.0 ± 11.6	23.5 ± 9.7	0.304
Hypoglycemia fear (HFS-II-SF sum score, range: 0-44)	15.0 ± 9.2	16.8 ± 9.9	0.361
Fear of complications (FCQ-SF sum score, range: 0-18)	9.4 ± 4.9	10.0 ± 5.0	0.561
<i>Patient-reported outcomes (17-day EMA phase)</i>			
Daily diabetes distress score (range: 0-100)	25.4 ± 17.4	30.3 ± 18.5	0.188
Daily hypoglycemia distress score (range: 0-100)	20.7 ± 12.8	17.7 ± 13.5	0.276
Daily hyperglycemia distress score (range: 0-100)	42.4 ± 18.4	49.4 ± 21.0	0.080
Daily variability distress score (range: 0-100)	34.7 ± 17.9	37.9 ± 15.0	0.391
<i>CGM-derived parameters of glycemic management (17-day EMA phase)</i>			
Mean glucose (mg/dl)	175.3 ± 38.6	193.0 ± 35.3	0.046
% <70 mg/dl (3.9 mmol/l)	3.8 ± 4.0	3.4 ± 2.8	0.642
% 70-180 mg/dl (3.9-10 mmol/l)	55.2 ± 17.2	47.6 ± 13.8	0.053
% >180 mg/dl (10 mmol/l)	41.0 ± 18.8	49.1 ± 15.0	0.061
Glucose fluctuations (CV)	32.0 ± 4.8	34.0 ± 4.8	0.070
Data reported as M±SD or n (%). # CGM use: real-time CGM or intermittent-scanning CGM; + list of complications: retinopathy, neuropathy, nephropathy, diabetic foot syndrome, cardiovascular disease, apoplex, arterial vascular disease; PAID = Problem Areas in Diabetes questionnaire; CES-D = Centre for Epidemiological Studies – Depression Scale; HFS-II-SF = Hypoglycemia Fear Scale – second edition – short-form; FCQ-SF = Fear of Complications Questionnaire – short-form; CV = Coefficient of Variation			

Supplementary Table S6. Sensitivity analysis: Associations with adherence to EMA signals

	Adherence (% of EMA prompts answered)	p-value
Age (in years)	$r = 0.187$	0.008
Gender	$r = -0.018$	0.796
Body-mass index (in kg/m ²)	$r = 0.139$	0.048
Years of education	$r = 0.116$	0.098
Duration of diabetes (in years)	$r = 0.120$	0.087
HbA1c (in %, [mmol/mol])	$r = -0.102$	0.147
Insulin pump therapy	$r = 0.107$	0.127
CGM [#] use prior to inclusion	$r = 0.088$	0.212
Long-term complications ⁺ (mean per person)	$r = 0.018$	0.800
<i>Patient-reported outcomes (Baseline assessment)</i>		
Diabetes distress (PAID sum score, range: 0-100)	$r = -0.043$	0.540
Depressive symptoms (CES-D sum score, range: 0-60)	$r = -0.052$	0.460
Hypoglycemia fear (HFS-II-SF sum score, range: 0-44)	$r = -0.058$	0.412
Fear of complications (FCQ-SF sum score, range: 0-18)	$r = -0.109$	0.123
<i>Patient-reported outcomes (17-day EMA phase)</i>		
Daily diabetes distress score (range: 0-100)	$r = -0.097$	0.167
Daily hypoglycemia distress score (range: 0-100)	$r = 0.081$	0.253
Daily hyperglycemia distress score (range: 0-100)	$r = -0.108$	0.125
Daily variability distress score (range: 0-100)	$r = -0.090$	0.199
<i>CGM-derived parameters of glycemic management (17-day EMA phase)</i>		
Mean glucose (mg/dl)	$r = -0.186$	0.009
% <70 mg/dl (3.9 mmol/l)	$r = 0.037$	0.603
% 70-180 mg/dl (3.9-10 mmol/l)	$r = 0.194$	0.007
% >180 mg/dl (10 mmol/l)	$r = -0.186$	0.009
Glucose fluctuations (CV)	$r = -0.088$	0.223
Depicted are Pearson correlation coefficients. # CGM use: real-time CGM or intermittent-scanning CGM; + list of complications: retinopathy, neuropathy, nephropathy, diabetic foot syndrome, cardiovascular disease, apoplex, arterial vascular disease; PAID = Problem Areas in Diabetes questionnaire; CES-D = Centre for Epidemiological Studies – Depression Scale; HFS-II-SF = Hypoglycemia Fear Scale – second edition – short-form; FCQ-SF = Fear of Complications Questionnaire – short-form; CV = Coefficient of Variation		

Supplementary Table S7. Sensitivity analyses with prior use of a CGM system before the study vs. new use of a CGM system

Predictor	Daily diabetes distress (range: 0-100)		Daily hypoglycemia distress (range: 0-100)		Daily hyperglycemia distress (range: 0-100)		Daily glucose variability distress (range: 0-100)	
	no prior CGM use (n=26)	prior CGM use (n=152)	no prior CGM use (n=26)	prior CGM use (n=152)	no prior CGM use (n=26)	prior CGM use (n=152)	no prior CGM use (n=26)	prior CGM use (n=152)
<i>Within-level predictors (daily assessment)</i>								
% <70 mg/dl (<3.9 mmol/l) +	0.13 (0.003 – 0.25)	0.03 (-0.02 – 0.09)	0.33 (0.19 – 0.45)	0.25 (0.19 – 0.30)	-0.17 (-0.28 – -0.05)	-0.04 (-0.09 – 0.00)	0.11 (-0.02 – 0.24)	0.01 (-0.05 – 0.07)
% >180 mg/dl (>10 mmol/l) +	0.44 (0.29 – 0.54)	0.40 (0.34 – 0.44)	0.01 (-0.15 – 0.15)	-0.10 (-0.15 – -0.05)	0.56 (0.46 – 0.63)	0.57 (0.54 – 0.61)	0.45 (0.34 – 0.54)	0.29 (0.23 – 0.35)
Glucose CV+	0.13 (0.02 – 0.23)	0.13 (0.07 – 0.18)	0.14 (0.02 – 0.26)	0.12 (0.08 – 0.17)	0.18 (0.09 – 0.27)	0.19 (0.14 – 0.22)	0.23 (0.12 – 0.32)	0.19 (0.15 – 0.24)
Number of glucose scans	-0.03 (-0.18 – 0.07)	0.10 (0.03 – 0.16)	0.22 (0.01 – 0.36)	0.20 (0.14 – 0.27)	-0.09 (-0.21 – 0.02)	0.06 (-0.01 – 0.12)	0.04 (-0.09 – 0.15)	0.14 (0.05 – 0.21)
<i>Between-level predictors (baseline assessment or person-average of the 17-day period)</i>								
Female gender	-0.29 (-0.89 – 0.28)	0.22 (-0.09 – 0.47)	-0.14 (-0.73 – 0.49)	-0.06 (-0.36 – 0.23)	-0.14 (-0.80 – 0.42)	0.22 (-0.14 – 0.51)	-0.20 (-0.78 – 0.33)	0.03 (-0.33 – 0.35)
Diabetes Distress (PAID sum score, range: 0-100)	0.11 (-0.52 – 0.86)	0.37 (0.02 – 0.63)	-0.70 (-1.36 – 0.03)	0.14 (-0.20 – 0.50)	-0.06 (-0.67 – 0.73)	0.37 (0.07 – 0.68)	-0.24 (-0.91 – 0.45)	0.07 (-0.23 – 0.34)
Depressive Symptoms (CES-D sum score, range: 0-60)	-0.57 (-1.24 – 0.40)	0.02 (-0.33 – 0.34)	-1.15 (-1.83 – -0.21)	0.12 (-0.27 – 0.53)	-0.71 (-1.45 – 0.16)	0.12 (-0.20 – 0.43)	-0.84 (-1.56 – 0.03)	-0.02 (-0.37 – 0.29)
Interaction PAID x CES-D	0.65 (-1.00 – 1.66)	0.12 (-0.31 – 0.61)	1.76 (0.22 – 2.85)	0.06 (-0.50 – 0.59)	0.81 (-0.74 – 1.92)	-0.26 (-0.74 – 0.17)	1.07 (-0.17 – 2.14)	0.27 (-0.17 – 0.71)
Person-average % <70 mg/dl (<3.9 mmol/l) +	-0.18 (-0.55 – 0.35)	0.05 (-0.13 – 0.23)	-0.15 (-0.53 – 0.35)	-0.31 (-0.47 – -0.09)	-0.10 (-0.54 – 0.49)	-0.08 (-0.27 – 0.13)	-0.32 (-0.64 – 0.30)	-0.16 (-0.35 – 0.03)

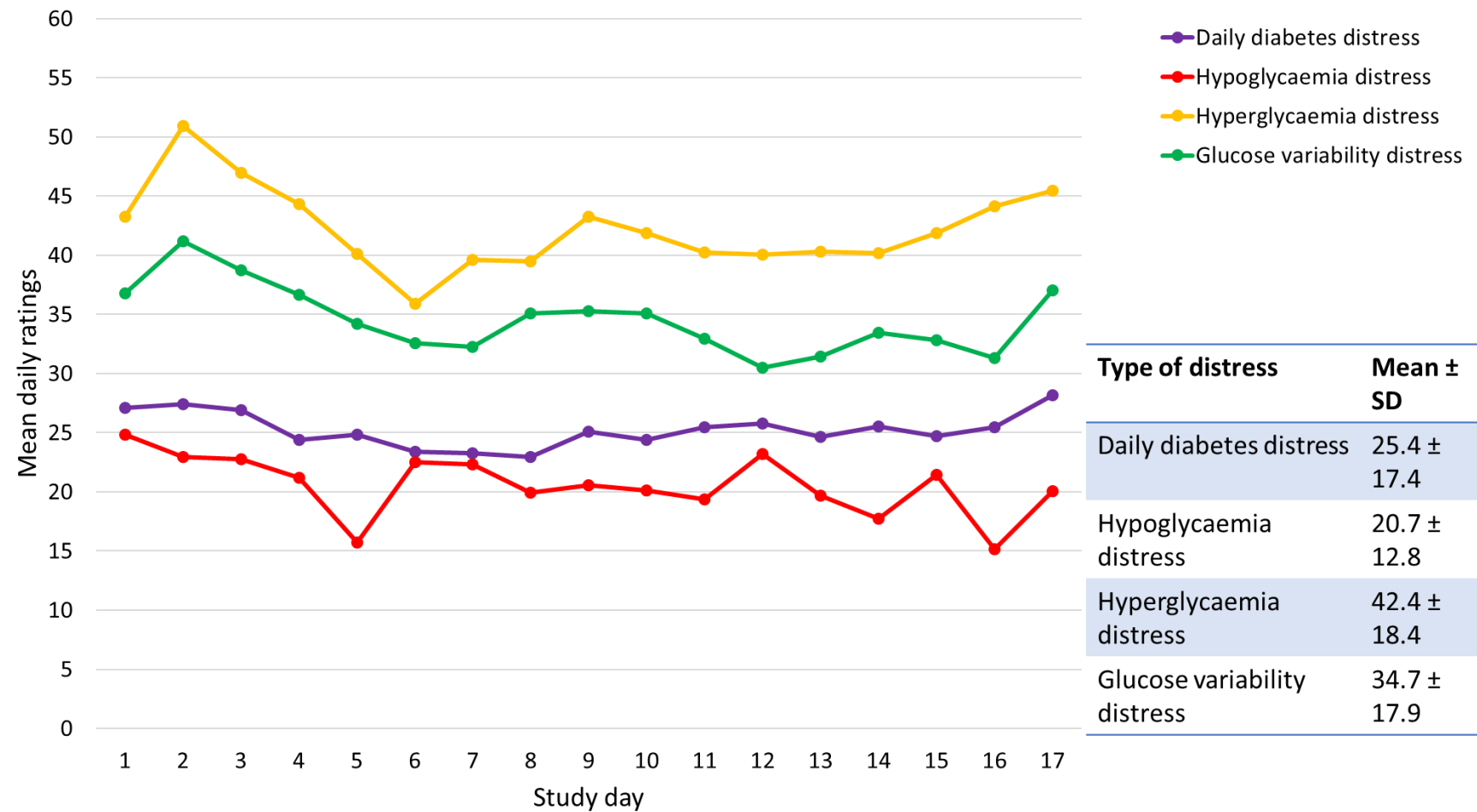
Supplementary Table S8. Sensitivity analyses with number of scans as dependent variable

Predictors of daily number of scans in separate analyses	Estimate (SD)	Standardized coefficient (95% confidence interval)
Effect of time only → number of glucose scans		
Study day	-0.185 (0.02)	-0.14 (-0.16 – -0.10)
Daily diabetes distress + Time in Range → number of glucose scans		
Study day	-0.20 (0.03)	-0.15 (-0.18 – -0.11)
Daily diabetes distress rating	0.02 (0.01)	0.05 (0.004 – 0.12)
Time in Range (70-180 mg/dl; 3.9-10 mmol/l) +	0.11 (0.05)	0.04 (0.001 – 0.08)
Daily hypoglycemia distress + Time in hypoglycemia → number of glucose scans		
Study day	-0.19 (0.02)	-0.14 (-0.17 – -0.11)
Daily hypoglycemia distress	0.03 (0.01)	0.13 (0.09 – 0.18)
% < 70 mg/dl (3.9 mmol/l) +	0.63 (0.18)	0.07 (0.02 – 0.10)
Daily hyperglycemia distress + Time in hyperglycemia → number of glucose scans		
Study day	-0.18 (0.02)	-0.13 (-0.13 – -0.10)
Daily hyperglycemia distress	0.02 (0.01)	0.07 (0.03 – 0.12)
% > 180 mg/dl (10 mmol/l) +	-0.30 (0.07)	-0.11 (-0.16 – -0.06)
Daily glucose variability distress + Glucose variability → number of glucose scans		
Study day	-0.17 (0.02)	-0.13 (-0.15 – -0.10)
Daily glucose variability distress	0.02 (0.01)	0.07 (0.03 – 0.12)
Glucose CV+	1.20 (0.16)	0.18 (0.15 – 0.21)
N=178. Two-level regression analysis using Bayes estimation with participant as nesting factor, daily number of glucose scans as criterion and within-level and between-level variables as predictors. Each analysis was controlled for study day and first autoregressive parameter as well as the person-average of distress ratings and glucose parameters for the 17-day period. + Unit of glucose parameters in decrements of 10%. CV = coefficient of variation. Significant findings (p < 0.05) in bold.		

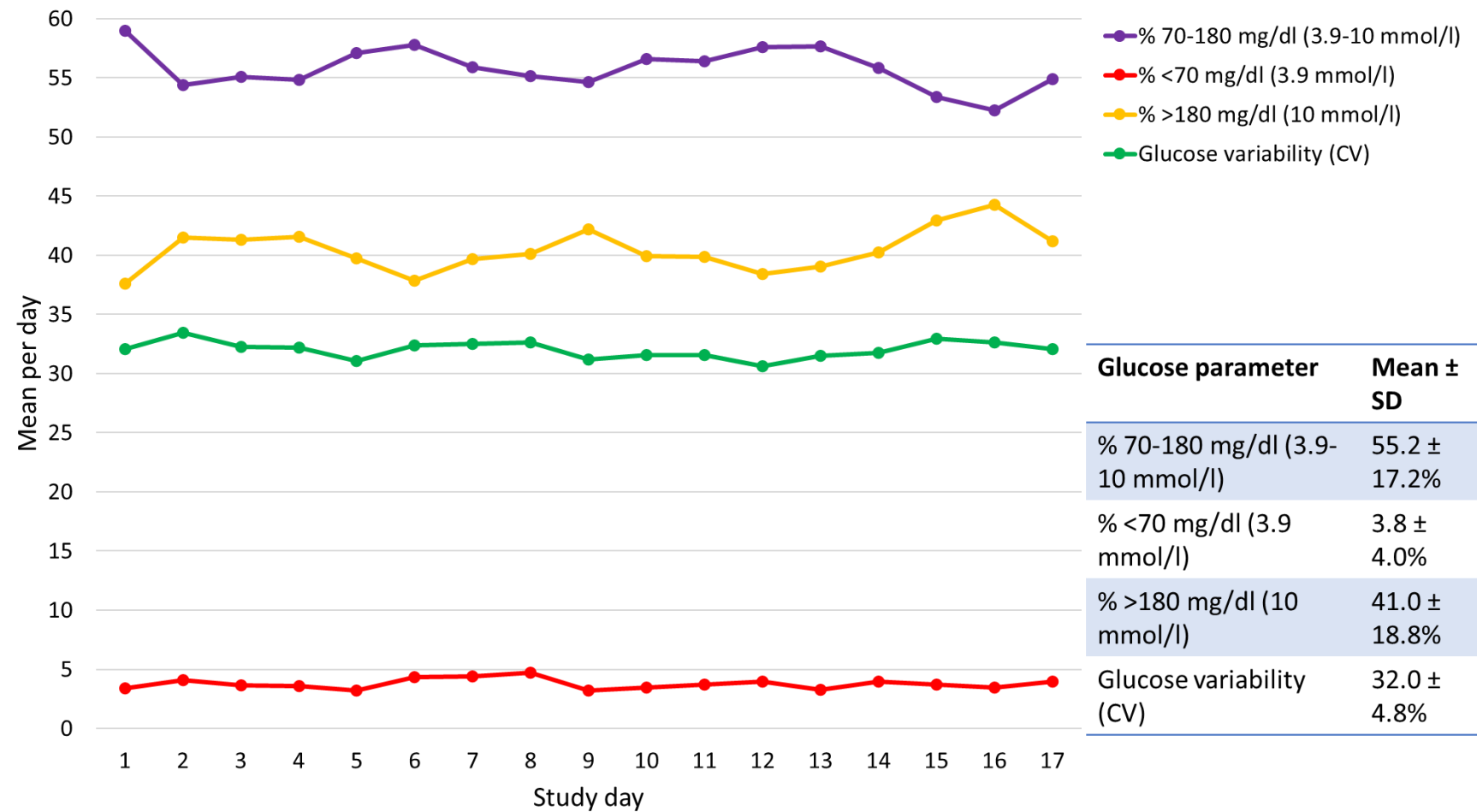
Supplementary Table S9. Sensitivity analyses with elevated vs. non-elevated baseline diabetes distress

Predictor	Daily diabetes distress (range: 0-100)		Daily hypoglycemia distress (range: 0-100)		Daily hyperglycemia distress (range: 0-100)		Daily glucose variability distress (range: 0-100)	
	baseline PAID < 40 (n=85)	baseline PAID ≥ 40 (n=93)	baseline PAID < 40 (n=85)	baseline PAID ≥ 40 (n=93)	baseline PAID < 40 (n=85)	baseline PAID ≥ 40 (n=93)	baseline PAID < 40 (n=85)	baseline PAID ≥ 40 (n=93)
<i>Within-level predictors (daily assessment)</i>								
% <70 mg/dl (<3.9 mmol/l) ⁺	0.10 (0.03 – 0.16)	0.01 (-0.05 – 0.07)	0.25 (0.19 – 0.32)	0.29 (0.21 – 0.35)	-0.05 (-0.12 – 0.02)	-0.07 (-0.13 – -0.01)	0.05 (-0.03 – 0.11)	0.00 (-0.07 – 0.08)
% >180 mg/dl (>10 mmol/l) ⁺	0.40 (0.32 – 0.47)	0.39 (0.32 – 0.45)	-0.08 (-0.18 – -0.01)	-0.07 (-0.14 – -0.01)	0.56 (0.50 – 0.61)	0.58 (0.53 – 0.62)	0.36 (0.28 – 0.42)	0.32 (0.25 – 0.38)
Glucose CV ⁺	0.08 (0.02 – 0.16)	0.14 (0.07 – 0.20)	0.13 (0.05 – 0.18)	0.14 (0.06 – 0.22)	0.18 (0.12 – 0.23)	0.19 (0.14 – 0.25)	0.22 (0.16 – 0.27)	0.22 (0.15 – 0.27)
Number of glucose scans	0.09 (-0.02 – 0.24)	0.03 (-0.04 – 0.14)	0.22 (0.15 – 0.31)	0.15 (0.06 – 0.23)	0.03 (-0.05 – 0.11)	0.02 (-0.06 – 0.09)	0.13 (0.04 – 0.22)	0.14 (0.07 – 0.21)
<i>Between-level predictors (baseline assessment or person-average of the 17-day period)</i>								
Female gender	0.07 (-0.49 – 0.51)	0.11 (-0.31 – 0.56)	0.12 (-0.35 – 0.46)	-0.18 (-0.58 – 0.29)	0.15 (-0.32 – 0.56)	0.15 (-0.28 – 0.62)	0.12 (-0.31 – 0.57)	-0.05 (-0.51 – 0.37)
Depressive Symptoms (CES-D sum score, range: 0-60)	0.09 (-0.12 – 0.30)	0.17 (-0.10 – 0.35)	0.02 (-0.18 – 0.22)	0.30 (0.12 – 0.49)	0.03 (-0.18 – 0.23)	-0.06 (-0.24 – 0.13)	-0.01 (-0.20 – 0.18)	0.28 (0.12 – 0.46)
Person-average % <70 mg/dl (<3.9 mmol/l) ⁺	-0.19 (-0.40 – 0.09)	0.08 (-0.20 – 0.36)	-0.32 (-0.53 – -0.05)	-0.32 (-0.55 – -0.01)	-0.13 (-0.38 – 0.16)	-0.10 (-0.39 – 0.22)	-0.22 (-0.44 – 0.07)	-0.22 (-0.43 – 0.12)
Person-average % >180 mg/dl (>10 mmol/l) ⁺	-0.18 (-0.42 – 0.09)	0.07 (-0.19 – 0.28)	-0.16 (-0.35 – 0.12)	-0.19 (-0.41 – 0.06)	-0.37 (-0.59 – -0.10)	-0.34 (-0.54 – -0.13)	-0.36 (-0.57 – -0.10)	-0.33 (-0.52 – -0.10)
Person-average glucose CV ⁺	-0.02 (-0.23 – 0.21)	0.08 (-0.18 – 0.39)	0.04 (-0.16 – 0.28)	0.26 (-0.04 – 0.48)	-0.16 (-0.38 – 0.09)	0.00 (-0.28 – 0.25)	-0.09 (-0.32 – 0.14)	0.21 (-0.03 – 0.45)

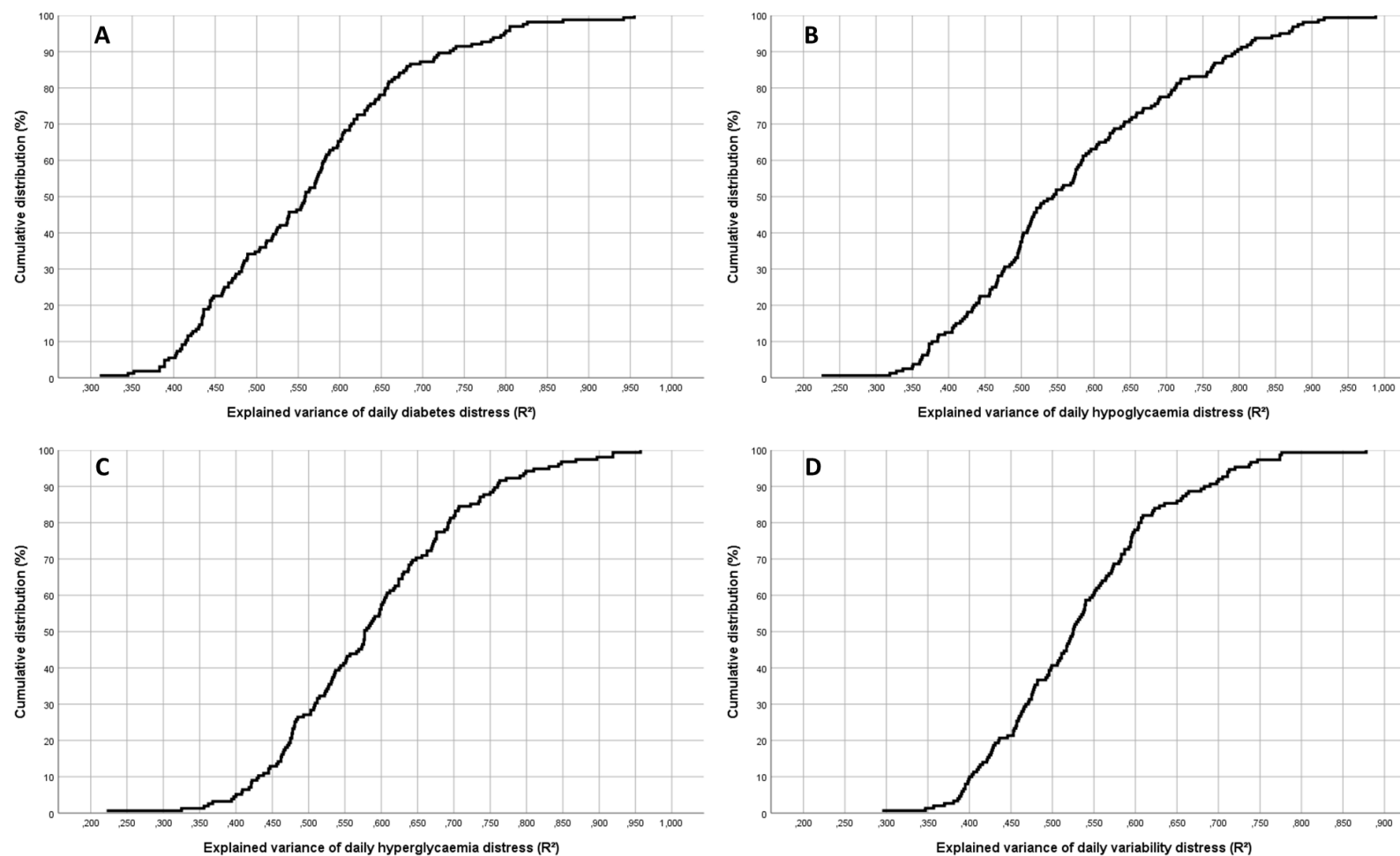
Supplementary Figure S1. Course of daily diabetes distress and glycemia-specific distress ratings across the 17-day study period.



Supplementary Figure S2. Course of CGM-derived glucose parameters across the 17-day study period.



Supplementary Figure S3. Cumulative distribution* of explained variance of daily diabetes distress (A), daily hypoglycemia distress (B), daily hyperglycemia distress (C), and daily variability distress (D).



*For each person, N=1 analyses were performed with the respective daily distress rating as dependent variable and the following variables as independent variables: % <70 mg/dl (3.9 mmol/l), % >180 mg/dl (10 mmol/l), Glucose-CV, study day, and first autoregressive parameter of the dependent variable.

Supplementary Figure S4. Different levels of associations between hyperglycemic exposure and daily hyperglycemia distress ratings in three N-of-1 analyses. Person A shows a high level of association; Person B shows a low level of association with fluctuating distress ratings while low exposure to hyperglycemic values; Person C shows a low level of association with no hyperglycemia distress but fluctuating exposure to hyperglycemic glucose values.

